CHAPTER 1

INTRODUCTION

1.1 Background

Severe acute respiratory syndrome coronavirus (SARS-CoV-2) is a new variant of coronavirus that caused an ongoing pandemic of coronavirus disease 2019 (COVID-19) (Naqvi et al., 2020). As of May 2022, the pandemic reported approximately 519 million cases and 6.3 million deaths globally (World Health Organization, 2022). A variety of studies and research are taken to provide a look into both preventive and curative measures against the SARS-CoV-2 virus. SARS-CoV-2 is a RNA virus from betacoronavirus of *Coronaviridae* family. Its genome is 26 to 32 kb in length, with characteristics of positive single-stranded, spiked, and enveloped (Zheng, 2020). As of 18 May 2022, WHO reported a total of two currently circulating variants of concern (VOC), three previously circulating VOCs, eight previously circulating variants of interest (VOI), and one variant under monitoring (VUMs) of SARS-CoV-2 (World Health Organization, 2022). Different variants manifest different symptoms with different levels of severity and transmissibility. Typical symptoms range from cough, fever, and sore throat. It may also develop into respiratory tract disease, which now has become the biggest contributing factor to the mortality number (Lee et al., 2020).

Belonging to the same *Coronaviridae* family, the human common cold coronavirus has been going around for decades. However, unlike COVID-19, it is well-known that the common cold coronavirus does not manifest serious signs and symptoms (Nelde et al., 2021). Some common cold coronaviruses infecting humans are 229E and NL63 from the alphacoronavirus, HKU1, and OC43 from the betacoronavirus (Poland, Ovsyannikova, & Kennedy, 2020).

Cross-reactivity refers to unanticipated reactivity towards another antigen that differs from the expected targets, possibly due to similar structural regions (Tomita et al., 2020). Pre-existing immunity may result in either protection or increased susceptibility toward SARS-CoV-2 (Lee et al., 2020). Several reports of SARS-CoV-2 cross-reactive T-cell in naïve individuals have been linked to

prior exposure to human common cold coronavirus (Altmann & Boyton, 2020; Sette & Crotty, 2021). Debates over the exact cause and mechanism are still going around. Some studies suggest that T-cell memory and reactivity might play some role in the process (Echeverría et al., 2021; Poland, Ovsyannikova, & Kennedy, 2020). Yet reports of contradictory findings where it is believed exposure to human common cold coronavirus does not primarily explain the cross-reactivity (Tan et al., 2021). Regardless of different opinions and arguments, understanding T-cell responses and reactivity is believed to be the key to understanding the disease responses to ensure suitable and effective control strategies are implemented (Grifoni et al., 2020; Vardhana et al., 2022).

In order for T-cells to exhibit responses, the T-cell receptor (TCR) has to recognize peptides that are presented by human leukocyte antigen (HLA) molecules (Abbas, Lichtman, & Pillai, 2020). However, it is a well-known fact that HLA molecules are population specific. Thus, different populations may present or possess different sets of alleles (Wieczorek et al., 2017). To date, most of the T-cell epitopes studies have originated from European and North American populations where their predominant HLA allotypes differ from Indonesian (Langton et al., 2021; Migliorini et al., 2021). The Indonesian HLA alleles are frequently neglected and not well-studied in research and published papers (Gustiananda, 2020). Thus, by primarily using HLA allotypes prevalent in Indonesia, this study hopes to gain more understanding and could be the starting point in identifying SARS-CoV-2 immunogenic epitopes and supporting cell-mediated immunity studies relevant for Indonesia populations.

Considering everything, this study hopes to identify potential cross-reactivity between SARS-CoV-2 and other human common cold coronaviruses in the context of T-cell epitopes peptides presented by HLA alleles of the Indonesian population through immunoinformatics approaches. Moreover, in the process, identifying conserved T-cell epitopes throughout the coronavirus family might help generate a universal vaccine construct (Zhao et al., 2016).

1.2 Objectives

The objectives of this study include:

a. To identify potential cross-reactivity between SARS-CoV-2 with other human common cold coronaviruses through epitope analysis.

b. To identify conserved T-cell epitopes throughout the coronaviruses family to generate potential candidates for universal coronavirus vaccine construct.